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EXAMINER	
MCKENZIE, THOMAS C	
ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 09/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,017	MIGAWA ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-34 and 37-44* is/are rejected.

7)☒ Claim(s) *35 and 36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to amendments filed on 7/22/04. Applicant has amended claims 38 and 44. Claims 2-34 and 37-44 were previously rejected. Claims 2-41 and 44 were designated as containing allowable subject matter. There are forty-three claims pending and forty-three under consideration. Claims 2-37 and 44 are compound claims. Claim 38 is a composition claim. Claims 42 and 43 are method of using claims. Claims 39-41 are method of making claims. This is the third action on the merits. The application concerns some antibiotic cytosine nucleoside analogue compounds, compositions, and uses thereof.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-34 and 37-44 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 44, page 8, lines 3, 5, 7, 10, 12, and 16, and in line 4, claim 2, page 2 Applicants claim "heteroalkyl" and "substituted heteroalkyl". In line 4, claim 44, page 8 they claim "alkyleneheteroalkyl". In line 6, claim 44 they claim, "heteroalkenyl". A "heteroalkenyl" radical is presumably an unsaturated version of a "heteroalkyl" radical; its structure is still unclear. What are these radicals? Nowhere in the

specification are they defined. In the passage spanning line 24, page 7 to line 8, page 8, Applicants define "alkyl". Lines 23-25, page defines "heterocycloalkyl" but there is no definition of heteroalkyl. There is a second and conflicting definition of "alkyl" in lines 16-19, page 11. The words "heteroalkyl", "substituted heteroalkyl", "alkyleneheteroalkyl", and "heteroalkenyl" are indefinite. There is no such thing. Is "heteroalkyl" an alkyl substituted by a heterocycle, e.g. pyridyl-methyl? An alkyl interrupted by a heteroatom, such as 2-ethoxyethyl? An alkyl substituted by a heteroatom, e.g. 2-chlorohexyl? Is "alkyleneheteroalkyl" an alkylenehetero attached to an alkyl, an alkylene attached to a heteroalkyl ring, or possibly an alkylene radical attached to a heteroatom, which in turn is attached to an alkyl group? Is "heteroalkenyl" an alkenyl radical substituted by a heterocycle, e.g. pyridyl-vinyl? A heterocycle linked through an alkenyl chain, 3-furanyl-1-propenyl? An alkenyl interrupted by a heteroatom, such as 3-ethoxy-2-propenyl? An alkenyl substituted by a heteroatom, e.g. 2-chloroallyl? Whatever choice is selected must be supported by the specification.

The Examiner suggests deleting "heteroalkyl", "substituted heteroalkyl", "alkyleneheteroalkyl", and "heteroalkenyl". Applicants cite a number of US Patents as containing the two terms "heteroalkyl" and "heteroalkenyl". Applicants also now define the term "heteroalkyl" as "a monovalent alkyl chain having at least

one heteroatom in the chain". They define "heteroalkenyl" as "a monovalent alkyl chain having at least one heteroatom and at least on carbon-carbon double bond as part of the chain". Finally, Applicants define "alkyleneheteroalkyl" as "an alkylene group that is substituted by a heteroalkyl moiety".

This is not persuasive. To the first point, the indefiniteness remains despite what was allowed in another case. The U.S. Court of Customs and Patent Appeals wrote *In re Giolito* 188 USPQ 645: "We reject appellants' argument that the instant claims are allowable because similar claims have been allowed in a patent. It is immaterial whether similar claims have been allowed to others. See *In re Margaroli,* 50 CCPA 1400, 318 F.2d 348, 138 USPQ 158 (1963); *In re Wright*, 45 CCPA 1005, 256 F.2d 583, 118 USPQ 287 (1958); *In re Launder*, 41 CCPA 887, 212 F.2d 603, 101 USPQ 391 (1954)".

To the second point, as laudable and clarifying as the proposed definitions are, they are not to be found in the specification as filed. Applicants are now choosing one of many possible definitions suggested by the Examiner. Where in the specification are guideposts pointing to these new definitions? The proposed definitions not the only ones possible and Applicants have not indicated why those definitions should be chosen from all the other possibilities. The mere existence of so many competing and contradictory definitions means that the terms

""heteroalkyl", "substituted heteroalkyl", "alkyleneheteroalkyl", and "heteroalkenyl" are indefinite.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42 and 43 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating bacterial infections, does not reasonably provide enablement for "administering" the composition generally. The specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The how to make requirement of the enablement statute, when applied to process claims, refers to operability and how to make the claimed process work. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*,

230 USPQ 546. To whom is the composition to be given? Is everyone, well or sick to be given the composition?

a) Determining if any particular claimed compound would treat every human disease would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it clinical trials with every different human disease, or to testing them in an assay known to be correlated to clinical efficacy of such treatment. This is a huge degree of experimentation. b) There is no direction concerning treating any diseases found in the specification. Applicants describe formulations in the passage spanning line 4, page 15 to line 2, line 30. There are no working examples of any formulation anywhere in this lengthy passage. Applicants do not teach the doses required to practice their invention anywhere in the specification. Since no compound has ever been used to treat every human disease, how is the skilled physician to know what dose to use for each of these different diseases? There is are *in vitro* assays drawn to 8 bacteria and 1 fungus species described in the passage spanning line 15, page 61 to the end of page 71. None of the tables of data are labeled with the microorganism used, so how is the physician to know which compound to use with which bacteria? A Table 3 is mentioned but is missing from the specification. c) There is no working example of treatment of any disease in man or animals. d) The nature of the invention is

clinical treatment of disease, which involves physiological activity. e) The state of the clinical arts is that no compound has ever been found that will "give a desired result" with every known disease.

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The scope of the claims involves all of the thousands of compounds of claim 1 as well as the uncounted number of diseases embraced by the claim. Thus, the scope of claims is very broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Applicants correctly surmise that the basis of this rejection is that it is not known to whom the "pharmaceutical composition" is to be administered, "in a pharmaceutically acceptable manner". Applicants then argue "[t]his decision is not a limitation to the present claim. Rather, such a decision is fully within the skill and discretion of one skilled in the art." This is not persuasive for two reasons. Firstly, the claim broadly reads on administering this to everyone, sick and well. It reads on administering this to people infected with bacteria as well as every other human disease. The MPEP in §2111 requires the Examiner to give the claim the, "broadest reasonable interpretation". Secondly, Applicants appear to be agreeing with the Examiner since there is no limitation concerning decision making by the physician who would use this claim. The claim as broadly interpreted is simply not operable and the claimed process will not work in the vast majority of people to whom the claim covers

Allowable Subject Matter

4. Claims 2-34, 37-41, and 44 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action. Claims 35 and 36 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

7. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (571) 272-0670. The FAX number for amendments is (703) 872-9306. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact Mukund Shah SPE of 1624 at (571)-272-0674.

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TCMcK/me